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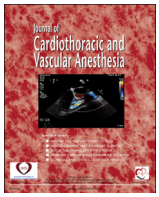

Original Article

Predicting the Necessity for Extracorporeal Circulation During Lung Transplantation: A Feasibility Study

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Objective: The factors leading to the implementation of unplanned extracorporeal circulation during lung transplantation are poorly defined. Consequently, the authors aimed to identify patients at risk for unplanned extracorporeal circulation during lung transplantation.

Design: Retrospective data analysis.

Setting: Single-center university hospital.

Participants: A development data set of 170 consecutive patients and an independent validation cohort of 52 patients undergoing lung transplantation.

Interventions: The authors investigated a cohort of 170 consecutive patients undergoing single or sequential bilateral lung transplantation without a priori indication for extracorporeal circulation and evaluated the predictive capability of distinct preoperative and intraoperative variables by using automated model building techniques at three clinically relevant time points (preoperatively, after endotracheal intubation, and after establishing single-lung ventilation).

Measurements and Main Results: Preoperative mean pulmonary arterial pressure was the strongest predictor for unplanned extracorporeal circulation. A logistic regression model based on preoperative mean pulmonary arterial pressure and lung allocation score achieved an area under the receiver operating characteristic curve of 0.85. Consequently, the authors developed a novel 3-point scoring system based on preoperative mean pulmonary arterial pressure and lung allocation score, which identified patients at risk for unplanned extracorporeal circulation and validated this score in an independent cohort of 52 patients undergoing lung transplantation.

Conclusions: The authors showed that patients at risk for unplanned extracorporeal circulation during lung transplantation could be identified by their novel 3-point score.

Key Words: lung transplantation; extracorporeal circulation; mathematical modeling; prediction model; automated model building techniques

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LUNG TRANSPLANTATION (LuTx) represents the life-saving surgical procedure for certain end-stage pulmonary diseases.[1] Although the majority of LuTx is performed without extracorporeal circulation (ECC), intraoperative hemodynamic instability as well as severely impaired gas exchange may trigger the implementation of ECC in 12% to 51% of all LuTx.[2–5] Unplanned ECC occurs in 12% of the cases potentially arising from sudden right-sided heart failure well after clamping of the pulmonary artery or from unexpectedly impaired gas exchange during single-lung ventilation.[2,4,6] Although pulmonary fibrosis and/or dilatation and hypertrophy of the right ventricle present risk factors for non-a priori ECC implementation,[3] there is no validated score to date that reliably identifies those patients who will require unplanned implementation of ECC during LuTx. In this feasibility study, the authors therefore set out to identify possible predictors based on various automated model building techniques and logistic regression using variables at three different clinical time points: preoperatively, after intubation, and during single-lung ventilation. Based on these analyses, the authors present a simple score that could help to identify patients at high risk for unplanned ECC implementation and may, therefore, serve as a tool to improve patients' safety during LuTx.

Methods

After approval by the local ethics board (approval number: 062-14), the authors first conducted an observational analysis on a training data set including all patients (n = 174) who received LuTx at the University Hospital Ludwig-Maximilians-University Munich between 2011 and 2013. Patients on ECC before or receiving a priori ECC at the beginning of the LuTx procedure (n = 4) were excluded from the analysis. The remaining set was comprised of 170 consecutive patients undergoing single (n = 67) or sequential bilateral LuTx (n = 103) without a priori indication for ECC. Of these, none of the single LuTx patients and 37 of the sequential bilateral LuTx patients needed ECC. Therefore, the authors additionally excluded single LuTx patients, leaving 103 sequential bilateral LuTx patients, who were grouped into the training data set. In a second step, the authors analyzed an independent cohort comprising all patients who underwent LuTx in 2014 (n = 23 single and n = 29 sequential bilateral LuTx) without a priori indication for ECC, who were grouped into the validation data set. The authors retrieved preoperative data and intraoperative digital anesthesia charts (Narkodata, IMESO, Germany). The primary surgical access route was extracted from the written surgical report. The lung allocation score (LAS) was calculated by means of the respective calculator on the homepage of Eurotransplant, which is responsible for the allocation of donor organs in Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands, and Slovenia. This international collaborative framework includes all transplant hospitals, tissue-typing laboratories, and hospitals where organ donations take place.[7] Factors contributing to the LAS calculation are listed in Table 1. Due to a change in the lung allocation system in December 2011, 4 patients listed as "high urgency" in the previous allocation system were arbitrarily assigned a novel LAS of 75. Variables with more than 10% missing values were excluded from the analysis. Three clinically relevant time points were defined for which a set of distinct variables were evaluated: (1) preoperatively, (2) after endotracheal intubation, and (3) after establishing either right-sided or left-sided single-lung ventilation (for the complete set of variables evaluated at each time point see Table 2). For each of these time points predictive capability was assessed as follows: using all variables available at that particular clinical time point (Table 2); patients from the training set were randomly split into five groups (5-fold cross validation). For each of the groups, the other four groups were merged and a logistic regression model was learned from the merged set by stepwise adding the available variables to the model, including the most significant one, and removing insignificant ones (stepwise forward logistic regression, Fig 1). Subsequently, model performance was measured by calculating the area under the receiver operating characteristic curve (ROC AUC) on the single, non-merged group. This procedure was repeated 20 times for each clinical time point with different random splits. Stepwise forward logistic regression used a p value of 0.05 as entry and exit criterion. Because the authors used a stepwise automated variable selection algorithm, interactions among variables were not evaluated. The final logistic regression model was derived using automated stepwise forward logistic regression on the full training data set. After derivation of the simplified, preoperative score, it was evaluated on the independent validation data set. All calculations were performed using R software 3.2.4 and corresponding packages (R Foundation for Statistical Computing, Vienna, Austria). Analyses of variance for

Table 1
Factors Contributing to Calculation of the Lung Allocation Score

Value	Unit
Date of birth	Day-month-year
Height	cm
Weight	kg
Lung diagnosis code	
Assistance level	No/some/total assistance
Diabetes	Insulin dependent/no diabetes/non-insulin-dependent/unknown
Assisted ventilation	Continuous mechanical/intermittent mechanical (no sedation)/noninvasive BiPAP or pressure support/noninvasive CPAP/not needed
Supplemental oxygen	At night/at rest/not needed/with exercise only
Amount of oxygen	F_IO_2 in %/l per min
FVC predicted	%
Pulmonary artery systolic pressure	mmHg
Mean pulmonary artery pressure	mmHg
Pulmonary capillary wedge mean	mmHg
Current PCO_2	kPa/mmHg
Highest PCO_2	kPa/mmHg
Lowest PCO_2	kPa/mmHg
→ Change in PCO_2	%
6-minute walk distance	Meters
Serum creatinine	mg per dl/μmol per l

Abbreviations: BiPAP, biphasic positive airway pressure; CPAP, continuous positive airway pressure; F_IO_2, fraction of inspired oxygen; FVC, forced vital capacity; PCO_2, partial pressure of carbon dioxide.

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